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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/620,178 | 07/15/2003 | Karel De Bruijn | 4-30602B-D1 | 8650 |

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

| EXAMINER | |
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| KRASS, FREDERICK F | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/620,178 | DE BRUIJN ET AL. | |
| | Examiner | Art Unit | |
| | Frederick Krass | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12/19/06 (RCE Filing)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *27, 35-48 and 50-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,35-48 and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/501,364.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/06; 6/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**Previous Rejections**

Unless specifically maintained/repeated infra, all previous rejections are withdrawn.

Because a new ground of rejection follows which was not necessitated by applicant's amendment, this action is NON-FINAL.

**Title**

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

**Specification: Reference to Priority Claim**

Applicant is requested to amend the first line of the specification to refer to the claims for priority to USSN 09/501,364, filed 02/19/2000 and now abandoned, and to PCT/EP99/06083, filed 08/19/1999.

**Specification: Trademarks**

The use of the following trademarks has been noted in this application:

1) "Polyplasdone XL USP/NF" (pages 20 and 22, line 2 of each; and page 24, lines 8 and 20); and

2) "Poloxalkol" (pages 20 and 22, line 4 of each; and page 24, lines 10 and 22).

The trademarks should be capitalized wherever they appear and be accompanied by generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

**Indefiniteness Rejection**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is incomplete insofar as it depends on a canceled claim.

**Obviousness Rejection**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) Claims 27, 35-40, 42-48 and 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giger et al (USP 5,510,353) in view of Catlow (USP 5,654,320), further in view of Batra et al (USP 7,060,294).

The primary reference discloses the use of the 5-$HT_4$ receptor antagonist 3-(5-methoxy-1H-indol-3yl-methylene)-N-pentylcarbazimidamide (compound "13" in Table 1 at column 14, a.k.a. tegaserod) as an antimotility agent for the treatment of gastrointestinal disturbances (column 25, lines 1 and 11). Administration may be via tablets containing "appropriate" solid carriers as taught at column 23, lines 18-23 and at column 24, lines 44 et seq. The prior art differs from the instant claims insofar as it does not specifically disclose the particular disintegrants recited instantly, in the percentages specified.

The secondary reference teaches using 5-HT4 receptor antagonists to treat, *inter alia*, gastrointestinal motility disorders (column 19, lines 15-25). It further teaches at column 19, lines 48-64 that conventional pharmaceutical auxiliaries can be broadly used:

> The usual methods of formulation used in pharmaceutical science and the usual types of compositions may be used, including tablets, chewable tablets, capsules, solutions, parenteral solutions, intranasal sprays or powders, troches, suppositories, transdermal patches and suspensions. In general, compositions contain from about 0.5% to about 50% of the compound in total, depending on the desired dose and the type of composition to be used. The amount of the compound, however, is best defined as the effective amount, that is, the amount of each compound which provides the desired dose to the patient in need of such treatment. The activity of the compounds do not depend on the nature of the composition, so the compositions are chosen and formulated solely for convenience and economy. Any compound may be formulated in any desired form of composition. Some discussion of different compositions will be provided, followed by some typical formulations.

Note that the two tablet working examples both use high amounts of disintegrants: formulation 2 (column 21) contains 94% starch; and formulation 3 contains 43.5% total disintegrant (as a combination of microcrystalline cellulose, polyvinylpyrrolidone and carboxymethyl starch). Tegaserod, the instantly claimed compound, is not specifically disclosed.

It would have been obvious to have incorporated relatively high amounts of disintegrants into the tablets of the primary reference for "convenience and economy", that being generally known from the secondary reference. The tablets suggested by the combined teachings of the primary and secondary references thus differ from those recited instantly insofar as the specific species of distintegrants recited instantly are not disclosed *ipsissima verba*.

The tertiary reference illustrates what is well-known, namely that the following components are conventional in the tablet formulation art: lactose filler (column 2, lines 23 and 24); carboxymethylcellulose calcium and sodium, crospovidone, sodium alginate, and pregelatinized starch distintegrants (column 2, lines 29-35); hydroxypropyl

methylcellulose binder (column 2, line 56); sodium lauryl sulfate and dioctylsuccinate surfactants (column 2, lines 60-64); and glyceryl monostearate and polyethylene glycol lubricants (see the passage bridging the last paragraph of column 3 and the first paragraph of column 4). Note the introductory paragraph of column 2, stating that the reference contemplates the use of "any" pharmaceutically acceptable fillers/compression aids, disintegrants, super-disintegrants, lubricants, binders, surfactants, film coatings and solvents. Since the tertiary reference is merely cited to demonstrate the general state of the tablet formulation art, it should be apparent that the prior art differs from the instant claims in its silence regarding tegaserod.

Generally, it is prima facie obvious to select a known material for incorporation into a composition, based on its recognized suitability for its intended purpose. *See* Sinclair & Carroll Co. v. Interchemical Corp., 325 US 327, 65 USPQ 297 (1945); see also In re Leshin, 227 F.2d 197, 125 USPQ 416 (CCPA 1960).

It would have been obvious to have used any of the various auxiliaries specifically recited by the instant claims in formulating the tablets suggested by the combined teachings of the primary and secondary references, motivated by the recognition of their suitability for that purpose by the tertiary reference, and consonant with the reasoning of the Sinclair and Leshin decisions.

Regarding claim 43, none of the prior art documents specifically disclose the particular dissolution characteristics recited therein. The instant fact situation is viewed, however, as being analogous to that of In re Greenfield, 197 USPQ 227 (C.C.P.A. 1978). In that case, certain paint additives were functionally characterized as being stable in the presence of formaldehyde. At page 229 of the decision, the court unambiguously stated

(despite the fact that the rejection was one of obviousness and not anticipation) that the burden was upon applicant to provide objective evidence of the existence of a degradation problem, i.e. the lack of such functionality in the prior art compositions (without relying solely on their specification).

The same rationale applies here. Applicant has characterized the instantly claimed products as having certain particular dissolution properties, but has provided no objective evidence that the presence of the particular disintegrants recited provides any unexpected dissolution characteristics.

2) Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Giger et al (USP 5,510,353) in view of Catlow (USP 5,654,320), further in view of Batra et al (USP 7;060,294) and Juch et al (USP 5,292,461).

The primary, secondary and tertiary references, and the rationale for combining their teachings, are provided supra. The tablets suggested by their combined teachings differ from the instant claim insofar as a polyoxyethylene-polyoxypropylene block co-polymer surfactant is not specified.

Poloxamers (a.k.a. polyoxyethylene-polyoxypropylene block copolymer surfactants) are well-known auxiliaries for use in tablet formulation. See Juchs et al (USP 5,292,461) at column 7, line 65. (The reference differs from the instant claims insofar as it is silent regarding tegaserod).

Again, it would have been obvious to have used a poloxamer as a surfactant in formulating the tablets suggested by the combined teachings of the primary, secondary

and tertiary references, motivated the recognition of their suitability for that purpose by Juch et al, consonant with reasoning of the Sinclair and Leshin decisions.

**Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick Krass whose telephone number is (571) 272-0580. The examiner can normally be reached at (571) 272-0580 on Monday through Friday from 9:30AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614